MASSIVE OSTEOLYSIS

A REVIEW OF SEVEN CASES

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Seven cases of massive osteolysis are presented. The aetiology of this disease is as yet unknown; neither age nor sex seems to be a factor in its incidence, nor are standard bone grafts or radiotherapy successful methods of treatment. However, in this series, operation produced a satisfactory outcome for five patients at a mean follow-up of 17 years; in three of these patients a custom-built prosthesis was inserted, and in one a conventional bone graft was combined with intramedullary nailing.

Spontaneous dissolution of bone was first reported by Jackson in 1838; since then a number of similar cases have been published under a wide variety of descriptive names, the most common of which are massive osteolysis (Gorham *et al.* 1954), acute spontaneous absorption of bone (Branch 1945), phantom bone (Gorham and Stout 1955) and disappearing or vanishing bones (Milner and Baker 1958).

In 1955 Gorham and Stout published a review of 24 cases, including two new cases of their own, and concluded that progressive osteolysis in those cases "was associated with an angiomasia of blood or lymphatic vessels"; this association is sometimes known eponymously as Gorham's disease. A second variety of adult osteolysis has also been described and is associated with either multiple lymphangiectases (Cohen and Craig 1955) or with haemangiomatosis (Jacobs and Kimmelstiel 1953; Fornasier 1970). In this variety there are multiple sites of disease and the soft-tissue disorder may spread to bone. Sometimes only a thin shell of cortical bone remains, and there is usually little replacement of the bone by fibrous tissue.

As well as unknown aetiology, the two varieties have several other characteristics in common. In both, the disease involves contiguous bones and standard biochemical and haematological tests are normal. Neither responds consistently to radiation therapy and neither metastasises, but encroachment on vital structures may occasionally be fatal. It is also well recognised that both may spontaneously regress (Edwards, Thompson and Varsa 1983). This paper reports one case of osteolysis in detail and reviews six previous cases from the records of the Bone Tumour Registry of the Royal National Orthopaedic Hospital.

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CASE REPORTS

Case 1. In 1980 a 14-year-old student went to see his general practitioner with a two-month history of pain in the posterior aspect of the right shoulder; there was a doubtful history of minor trauma about six months earlier. He was referred to the Middlesex Hospital where examination revealed a 3 cm hollow in the spine of the right scapula. There was minimal tenderness in the area but no bruit. There was no local lymphadenopathy and the adjacent shoulder joint had a full range of movement in all directions. The initial radiographs showed that the superior and medial aspects of the scapula and its spine were radiolucent; there was no other abnormality (Fig. 1). An open biopsy was performed using a posterior approach; this confirmed the absence of the scapular spine. Adjacent tissue sent for analysis revealed several sizeable vascular spaces, mainly with thin walls. There was also evidence of recent rapid resorption and new bone formation, an appearance consistent with vanishing bone disease.

As the lesion was thought not to be amenable to surgery, the patient was given radiotherapy (2000 rads) after the wound had healed. A CT scan taken at this time can be seen in Figure 2. Although radiotherapy had a beneficial effect on his symptoms, the osteolysis progressed and two years later the whole of the scapula and the contiguous distal clavicle were involved (Fig. 3). At this time he was re-admitted and a right percutaneous femoral arteriogram was performed in the hope of demonstrating, in the affected area, abnormal circulation which might be suitable for embolisation. Unfortunately, only a faint blush in the scapular region during the capillary phase was revealed (Fig. 4). A xerogram taken at the time clearly showed the clavicular involvement. However, a technetium bone scan taken during the same admission failed to reveal any increased activity in the area. No treatment was offered.

The patient continued under observation and, because of increased discomfort in the area, had another

Fig. 1

Fig. 2

Fig. 3

Fig. 4

Case 1. Figure 1—Radiograph of the right scapula at presentation, showing dissolution of the superior and medial aspects of the bone. Figure 2—A CT scan at the time of biopsy shows a clearly defined loss of the body and spine of the scapula. Figure 3—Further dissolution of the scapula with involvement of the contiguous distal clavicle. Figure 4—Arteriography of the right shoulder region shows the scapula outlined by a capillary blush; no abnormal circulation was detected. Figure 5—Further progress of the disease to involve most of the right clavicle.

Fig. 5

biopsy in January 1983; at the same operation a specimen of normal iliac bone was removed by trephining. Before anaesthesia his serum biochemistry estimation was again normal, as were the levels of serum parathyroid hormone, urinary calcium and phosphate excretion. The histological features of the biopsy were identical to those of the previous biopsy of September 1980, and the iliac bone was structurally normal.

Tissue and serum taken at the time of this biopsy were sent fresh to the Kennedy Institute at the Royal Postgraduate Medical School. Attempts to measure serum calcitonin levels, tissue culture techniques designed to reveal active osteoclasts and measurement of leucine aminopeptidase by histochemical techniques, all proved to be unrewarding. The patient was again offered no further treatment but was kept under observation. When last reviewed in March 1985 the osteolytic process was slowly but relentlessly progressing (Fig. 5).

A search of the Bone Tumour Registry at the Royal National Orthopaedic Hospital has revealed six similar cases.

Case 2. This patient, a 37-year-old student already reported by Poirier in 1968, had presented in 1962 with a six-month history of a painful right shoulder. The original radiographs suggested massive osteolysis but before biopsy could be performed a pathological fracture occurred in the upper humerus. Arteriography was normal. An open biopsy was performed, and eight weeks later a local resection and prosthetic replacement of the

upper three-quarters of the right humerus was performed. Histological examination of both the biopsy and the resected specimen revealed irregular fibrous tissue with large vascular spaces and dilated, thin-walled vascular channels, as well as evidence of active osteoclastic resorption. The patient made an uneventful recovery and has been reviewed regularly. In July 1984 there was no evidence of any local recurrence of the disease, although the lower end of the prosthesis had perforated the humeral cortex and presumably was loose. Elbow flexion at this time was 0° to 90° with full supination and pronation.

Case 3. This case was described by Aston in 1958. A 24-year-old woman presented with a three-year history of pain in the lateral aspect of her left thigh. Clinical examination was unrewarding but a radiograph revealed an area of osteolysis in the upper third of the femoral shaft. A biopsy was performed, after which she sustained a pathological fracture. Histological examination revealed cavernous sinusoidal vascular tissue. The area was bone-grafted but the grafts resorbed. In July 1957 an above-knee amputation was performed; the upper femur was resected and replaced by a prosthetic implant to provide a stump for an artificial limb. As in Case 2 haemangiomatosis was confirmed histologically. The patient was reviewed in March 1985 when there was no evidence of recurrent disease.

Case 4. In 1973 a 19-year-old female with a six-month history of mild pain in the lower right femur suffered a

Table I. Clinical details, histology and treatment of osteolytic lesions in seven patients

Case	Age	Sex	Site	Presenting symptoms	Histological confirmation	Bone grafts	Other treatment
1	14	M	Scapula	Pain	Positive	Not used	Radiotherapy
2	37	M	Humerus	Pain and pathological fracture	Positive	Not used	Resection and prosthesis
3	24	F	Femur	Pain and pathological fracture	Positive	Resorbed	Resection and prosthesis
4	19	F	Femur	Pain and pathological fracture	Positive	Resorbed	Resection and prosthesis
5	59	M	Femur	Pathological fracture	Positive (generalised)	Resorbed	Amputation
6	58	F	Humerus	Pain and pathological fracture	Negative	Successful	Intramedullary nail
7	56	F	Ribs	Pain	Positive	Not used	Radiotherapy

pathological fracture in the supracondylar region. A biopsy was performed and histological examination again revealed abnormal sinusoidal blood vessels, mainly thin-walled. Bone grafting was performed but the graft resorbed. Later the same year the lower femur was resected distal to the fracture site and was replaced by an implant linked to a Stanmore knee prosthesis. When last reviewed in July 1984 there was no sign of any recurrence and the right knee could be flexed from 0° to 90° with no quadriceps lag.

Case 5. This case of cutaneous haemangiomatosis in a 59-year-old man who had presented with a pathological fracture of the right femur, was previously reported by Fornasier (1970). Radiological investigation revealed diffuse osteolysis, both at the fracture site and in the contralateral femur. The left femur was treated prophylactically by Küntscher nailing, while the fracture of the right femur was explored, biopsied and also treated by insertion of a Küntscher nail. The biopsy showed friable tissue, identical in both soft tissue and bone; there were intercommunicating vascular channels, often with a thin and attenuated lining, and the overall appearance was thought to be consistent with vanishing bone disease. Because the patient bled copiously after the operation, an above-knee right amputation was performed. The histological appearances in this specimen were identical to those described in the biopsy. When last reviewed in 1976, the patient had no signs of recurrent disease but has since been lost to follow-up.

Case 6. A 58-year-old woman presented with a pathological fracture in the upper third of the right humerus after a six-month history of mild discomfort. Exploration of the fracture revealed little definitive tissue, and the humerus was grafted and stabilised with an intramedullary Küntscher nail. After six months the fracture united. Two years after operation the shoulder had only 60° of abduction but elbow function was normal. There was a suspicion of recurrent disease but the patient has not been seen since 1977.

Case 7. A 56-year-old woman presented with a six-month history of aching discomfort in the right side of her rib cage. The onset of her symptoms stemmed from a minor injury for which she had sought no treatment. No diagnosis was made at the initial visit, and she was

treated with physiotherapy without success. At review a radiograph revealed osteolysis in the lateral and posterior ribs on the right side. Haematological and biochemical tests were normal, as was a bone scan, but the osteolysis nevertheless rapidly involved the upper scapula and the outer right clavicle. In June 1980, 18 months after the onset of symptoms, an open biopsy was performed; this revealed marked osteoclastic activity with thinning of the contiguous cortical bone. The absent bone was replaced by a thin layer of fibrous disease. The patient received a course of radiotherapy (3000 rads) but the osteolysis progressed along the clavicle. The patient died in 1984 of cardiorespiratory failure.

DISCUSSION

It is now clearly established that the angiomatous process of massive osteolysis is pathologically different from haemangioma of bone (Gorham *et al.* 1954). This review of seven cases confirms that the process is usually confined to a specific area of bone but may occasionally be generalised and associated with multiple cutaneous haemangiomas (Fornasier 1970).

In a review of the literature published since 1938, Sacristan *et al.* (1977) found 60 reported cases of massive osteolysis, of which only four involved the scapula (Branch 1945; Gorham *et al.* 1954; Caulet *et al.* 1968). Since his review, a fifth case of scapular osteolysis in a 15-year-old boy has been reported by Heyden, Kindblom and Nielsen (1977); in this patient, although the majority of the right scapula was destroyed, there was no involvement of the adjacent bones. Case 1 of the present series thus seems to be the sixth reported case of scapular osteolysis; however, here the process also involved the clavicle, though not the ribs, and it continues to progress despite attempts at treatment. In these last two cases, operation revealed replacement of bone by dense vascular fibrous tissue, and histological findings in both cases were identical.

The results of this review are summarised in Table I. Although the disease was thought to occur only in adolescents and young adults (Sage and Allen 1974), this cannot be confirmed by the present review; nor does the patient's sex seem a significant factor. Mild pain was a presenting feature in all seven patients and a pathological

fracture occurred in five. In only three patients was there a history of minor trauma, and there was no evidence that the pathology was related to traumatic osteolysis, which is not infrequently seen in the distal clavicle in athletes (Jacobs 1964).

The radiological appearances in patients with osteolytic limb bones were consistent with the findings of Torg and Steel (1969). They described the first recognisable change as a diffuse osteolysis, possibly followed by a pathological fracture. In the second stage there may be increasing deformity, even without fracture, and loss of bone mass. During the third stage the osteolysis may involve the adjacent soft tissues or spread across joints to contiguous bones. Lastly, there is a phase of concentric shrinkage of the bone ends; these, they suggest, come to resemble "sucked candy". At no stage is there any evidence of bone regeneration. In this review a CT scan was available only in Case 1; this provided excellent delineation of the scapula, an area often poorly visualised by standard radiological views. A technetium bone scan performed on the same patient provided no more information of clinical value. Xerography was likewise unhelpful.

Arteriography was performed in two patients (Cases 1 and 2) to detect abnormal circulation in the affected areas. The faint capillary blush seen in Case 1 was disappointing, as therapeutic embolisation could not then be considered as a mode of treatment; this method had been used previously in treating surgically inaccessible tumours (Channon and Williams 1982). In no patient was direct injection of contrast medium into the abnormal area attempted, although this has been used to outline an absorbed scapula (Hambach, Pujman and Malý 1958).

Because of the rarity of this disease and the known possibility of spontaneous arrest (Kery and Wouters 1970), assessment of any method of treatment is difficult. After reviewing the available literature, Johnson and McClure (1958) suggested that radiotherapy should be the initial treatment, with operation reserved for unresponsive cases. Unfortunately, several such have already been documented (Hambach *et al.* 1958; Halliday *et al.* 1964; Wallis, Asch and Maisel 1964), and Cases 1 and 7 of this report also were resistant to radiotherapy.

Operative treatment is essentially a choice between amputation and local resection. If the latter is chosen, a bone graft, with or without internal fixation, or a custom-built prosthesis may be inserted (Burrows, Wilson and Scales 1975). Standard bone-grafting techniques give poor results in osteolysis (Bullough and Goodfellow 1976; Rosenquist and Wolfe 1968; Woodward, Chan and Lee 1981), and in this series, three of four bone grafts were resorbed. One patient, however (Case 6), did have successful reconstitution of the proximal humerus when conventional bone grafting was combined with intramedullary nailing and limited local

resection. Picault *et al.* (1984) have recently reported successful reconstruction of a femur affected by idiopathic osteolysis using a vascularised fibular graft; this, too, was combined with only a limited resection of the osteolytic area. If vascularised grafts are truly resistant to osteolysis, this may well become a useful method of treatment. Local resection and the insertion of custom-built prostheses was the technique used in three patients (Cases 2, 3 and 4). In all of these, there has been good preservation of limb function and no evidence of recurrent disease after 23, 28 and 12 years respectively. Case 3 was initially treated in 1957 and today would probably be treated by a sub-total femoral replacement combined with total hip arthroplasty. Massive prosthetic replacement may thus be considered in those cases of osteolysis which are resistant to radiation, peripherally sited and unifocal.

There is unfortunately no known treatment for those cases of radio-resistant disease which are inoperable (as in Cases 1 and 7). A rational approach would be first to consider the mechanisms producing the osteolysis and a number of theories have been proposed. Heyden *et al.* (1977) suggested that angiomatosis might induce local hypoxia and acidosis and that this might favour the activity of local hydrolytic enzymes. Such an environment may also induce the chelation of calcium ions (Nisbet, Helliwell and Nordin 1970). It must be stressed, however, that at open biopsy there is no macroscopic evidence of any avascularity. Sage and Allen (1974) suggest that osteolysis should be regarded as a locally aggressive condition, like a desmoid tumour, even though on occasions at biopsy virtually no tissue may be visible.

Using histochemical staining techniques, Heyden *et al.* (1977) found an increased activity of acid phosphatase and leucine aminopeptidase in perivascularly-arranged cells. These findings (which we could not confirm) led them to suggest that the source of the osteolysis may be a pericyte or osteoclast precursor. The relationship of these pre-osteoclasts to vascular networks has been studied by Scott (1967) who concluded that such progenitor cells were derived from mesenchymal cells which accompany capillary blood vessels. According to Bonucci (1981), the progenitor mononuclear lymphoid cells or pre-osteoclasts, once formed, reach the bone surface via the blood stream; they then form active osteoclasts. This conclusion that circulating pre-osteoclasts are involved in the osteolytic process is further supported by the observation that circulating monocytes in tissue culture are capable of both inducing and stimulating bone resorption (Dominguez and Mundy 1980). Unfortunately, tissue cultures from Case 1 of this series revealed no osteoclasts or monocytic cells resembling progenitor cells and also failed to produce any cells with osteoclastic potential. An alternative hypothesis is that osteolysis results from pathological stimulation of osteoclastic activity. A review of the available histology from six of the seven cases studied revealed no evidence of any osteoclastic proliferation. In

three patients, however (Cases 1, 2 and 7), there was good evidence of active osteoclastic resorption at the disease-bone interface.

Massive osteolysis may therefore represent a local derangement of osteoclastic activity, perhaps under the influence of a local stimulus (Mundy *et al.* 1978). The lack of symptoms or signs of acute inflammation would imply that prostaglandins, which are implicated in osteolysis associated with malignant disease (Samuel *et al.* 1980), are not involved in the idiopathic variety. Massive

osteolysis may then be akin to Paget's disease where there also seems to be a primary disorder of osteoclastic activity (Hosking 1981). In Paget's disease, osteoclastic function may be modified by treatment, and it seems reasonable to suggest that radio-resistant cases of massive osteolysis may in future be treated with sequential diphosphonates, calcitonin and mithramycin.

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